

Preliminary Amendment
Attorney Docket No.: 2578-6723US

IN THE CLAIMS:

Claims 19-26 have been cancelled. New claims 29-39 have been added. All claim amendments and cancellations are made without prejudice or disclaimer. Please enter the following claims:

1. (Currently amended) A binding molecule comprising an agonistic binding molecule capable of binding to and stimulating the human OX40-receptor.
2. (Currently amended) A-The binding molecule according to of claim 1, wherein the binding molecule is a human binding molecule.
3. (Currently amended) A-The binding molecule according to of claim 46 4 or 2, wherein the binding molecule comprises at least a CDR3 complementary determining region comprising the amino acid sequence selected from the group consisting of SEQ ID NO:17 (DRYSQVH~~Y~~ALDY), SEQ ID NO:18 (DRYVNTSNAFDY), SEQ ID NO:19 (DMSGFHE~~Y~~FDY), SEQ ID NO:20 (DRYFRQQN~~Y~~AFDY), SEQ ID NO:21 (ARAAGTIF~~Y~~DY), SEQ ID NO:22 (DRYITLPN~~Y~~ALDY), SEQ ID NO:23 (YDEPLTIYWFDS) and SEQ ID NO:24 (YDNVMGLYWFDY).
4. (Currently amended) A-The binding molecule according to any one of the claims 4-3 of claim 461, wherein the binding molecule comprises a heavy chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27 and SEQ ID NO:28.
5. (Currently amended) A-The binding molecule of claim 46, comprising a functional variant of a binding molecule according to claim 3 or 4 comprising at least one amino acid sequence selected from the group consisting of SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, and SEQ ID NO:28, wherein the functional variant

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is capable of competing for specifically binding to the human OX40-receptor.

6. (Currently amended) ~~An~~ The binding molecule of claim 46, wherein the binding molecule comprises an immunoconjugate comprising a binding molecule according to any one of the claims 1 – 4 or a functional variant according to claim 5, the immunoconjugate further comprising at least one tag.

7. (Currently amended) A nucleic acid sequence encoding ~~a~~ the binding molecule according to any one of the claims 1 – 4 or a functional variant according to claim 5 of claim 46.

8. (Currently amended) A vector comprising at least one nucleic acid sequence according to claim 7.

9. (Original) A host comprising at least one vector according to claim 8.

10. (Currently amended) ~~A~~ The host according to claim 9, wherein the host is a cell derived from a human cell.

11. (Currently amended) A method of producing a binding molecule capable of binding to and stimulating the human OX40-receptor, according to any one of the claims 1 – 4 or a functional variant according to claim 5, wherein the method comprises the steps of the method comprising:

(a) culturing a host comprising at least one vector encoding a binding molecule or functional variant thereof capable of binding to and stimulating the human OX40-receptor according to claim 9 or 10 under conditions conducive to the expression of the binding molecule or functional variant, and;

(b) optionally recovering the expressed expressing the binding molecule or functional variant; and

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isolating the binding molecule or functional variant.

12. (Currently amended) ~~A—The~~ binding molecule or functional variant thereof as obtainable by ~~, produced by the method~~ the method according to claim 11.

13. (Currently amended) A method of identifying a binding molecule capable of specifically binding to the human OX40-receptor or a nucleic acid molecule encoding a binding molecule specifically binding to the human OX40-receptor, ~~wherein the method comprises the steps of the method comprising:~~

- (a) — contacting a phage library of binding molecules with ~~material comprising the extracellular domain of the~~ human OX40-receptor,
- (b) — selecting at least once for a phage binding to the ~~material comprising the~~ human OX40-receptor, and
- (c) — separating and recovering the phage binding to the ~~material comprising the~~ human OX40-receptor.

14. (Currently amended) ~~A method of obtaining a binding molecule specifically binding to the human OX40 receptor or a nucleic acid molecule encoding a human binding molecule specifically binding to the human OX40 receptor, wherein the method comprises the steps of:~~

- (a) — ~~performing the~~ The method according to claim 13, and
- (b) — further comprising isolating from the recovered phage the binding molecule or the nucleic acid molecule encoding the binding molecule.

15. (Currently amended) A composition comprising ~~a—the~~ binding molecule of claim 46 according to any one of the claims 1—4, a functional variant according to claim 5, an immunoconjugate according to claim 6, or a binding molecule or functional variant thereof according to claim 12 and a stabilizing molecule.

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16. (Currently amended) A composition comprising ~~a—the nucleic acid molecule according to claim 7 and a gene delivery vehicle.~~

17. (Currently amended) A pharmaceutical composition comprising ~~a—the according to any one of the claims 1—4, a functional variant according to claim 5, an immunoconjugate according to claim 6, a binding molecule or functional variant thereof according to claim 12, or a composition according to claim 15 or 16, of claim 46 the pharmaceutical composition further comprising and~~ at least one pharmaceutically acceptable excipient.

18. (Currently amended) ~~A—The pharmaceutical composition according to claim 17 further comprising at least one other therapeutic agent.~~

19. – 26. (Cancelled)

27. (Currently amended) A method for modulating a T-cell response in a ~~human subject, said method comprising the step of administering to said human subject an effective dose of a composition comprising the binding molecule according to any one of the claims 1—4 or a functional variant of claim 5, an immunoconjugate according to claim 6, a nucleic acid molecule according to claim 7, a vector according to claim 8 or a pharmaceutical composition according to claim 17 or 18 of claim 1 in an amount sufficient to bind to and stimulate the OX40-receptor in the subject.~~

28. (Currently amended) ~~A—The method according to claim 27, wherein said modulation comprises the stimulation of T-cell proliferation.~~

29. (New) The method according to claim 27, wherein the subject is a human.

30. (New) The method according to claim 11, said method further comprising recovering the expressed binding molecule or functional variant.

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31. (New) The method according to claim 27, wherein the binding molecule comprises a complementary determining region comprising an oligopeptide sequence consisting of 10 to 12 amino acids, wherein the oligopeptide sequence is Xaa₁-Xaa₂-R-Xaa₃-Asp-Xaa₄, wherein Xaa₁ is selected from the group consisting of Ala, Tyr, and Asp, Xaa₂ is selected from the group consisting of Asp, Arg and Met, R is selected from the group consisting of a pentapeptide or a heptapeptide, Xaa₃ is Phe or Leu, and Xaa₄ is Tyr or Ser, wherein the binding molecule binds to and stimulates the OX40-receptor in the subject.

32. (New) The method according to claim 31, wherein the complementary determining region is selected from the group consisting of SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23 and SEQ ID NO:24.

33. (New) The method according to claim 31, wherein the binding molecule comprises a sequence selected from the group consisting of SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27 and SEQ ID NO:28.

34. (New) The method according to claim 31, wherein the binding molecule further comprises at least one tag that enhances an immune response in the subject.

35. (New) The method according to claim 31, wherein administering to said subject an effective dose of the binding molecule further comprises administering to said subject an effective dose of a nucleic acid sequence encoding the binding molecule, wherein the nucleic acid sequence is operably linked to a regulatory sequence, and expressing the binding molecule in the subject.

36. (New) The method according to claim 27, wherein the composition further comprises at least one pharmaceutically acceptable excipient.

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37. (New) The method according to claim 27, comprising enhancing an immune response in the subject.

38. (New) The method according to claim 37, comprising enhancing the immune response against a tumor, bacteria or viral antigen.

39. (New) A method of treating neoplastic, viral or bacterial diseases, the method comprising:

administering the binding molecule of claim 1 to a subject believed to be in need thereof.

40. (New) A method for modulating a T-cell response in a subject, comprising:
administering an effective dose of a binding molecule to a subject, wherein the binding molecule comprises a complementary determining region comprising an oligopeptide sequence consisting of 10 to 12 amino acids, wherein the oligopeptide sequence is Xaa₁-Xaa₂-R-Xaa₃-Asp-Xaa₄, wherein Xaa₁ is selected from the group consisting of Ala, Tyr, and Asp, Xaa₂ is selected from the group consisting of Asp, Arg and Met, R is selected from the group consisting of a pentapeptide or a heptapeptide, Xaa₃ is Phe or Leu, and Xaa₄ is Tyr or Ser;
binding the binding molecule to an OX40-receptor in the subject;
enhancing an immune response in the subject; and
stimulating the OX40-receptor, thereby modulating the T-cell response in the subject.

41. (New) The method according to claim 40, wherein the binding molecule comprises at least one amino acid sequence selected from the group consisting of SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, and SEQ ID NO:28.

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42. (New) The method according to claim 41, wherein the binding molecule comprises SEQ ID NO:25 and SEQ ID NO:29.
43. (New) The method according to claim 41, wherein the binding molecule comprises SEQ ID NO:26 and SEQ ID NO:30.
44. (New) The method according to claim 41, wherein the binding molecule comprises SEQ ID NO:27 and SEQ ID NO:31.
45. (New) The method according to claim 41, wherein the binding molecule comprises SEQ ID NO:28 and SEQ ID NO:32.
46. (New) The binding molecule of claim 1, wherein the binding molecule comprises a complementary determining region comprising an oligopeptide sequence consisting of 10 to 12 amino acids, wherein the oligopeptide sequence is Xaa₁-Xaa₂-R-Xaa₃-Asp-Xaa₄, wherein Xaa₁ is selected from the group consisting of Ala, Tyr, and Asp, Xaa₂ is selected from the group consisting of Asp, Arg and Met, R is selected from the group consisting of a pentapeptide or a heptapeptide, Xaa₃ is Phe or Leu, and Xaa₄ is Tyr or Ser.
47. (New) The nucleic acid of claim 7, wherein said nucleic acid molecule encodes a binding molecule having an amino acid sequence selected from the group consisting of SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28.
48. (New) The binding molecule of claim 5, comprising SEQ ID NO:25 and SEQ ID NO:29.
49. (New) The binding molecule of claim 5, comprising SEQ ID NO:26 and SEQ ID NO:30.

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50. (New) The binding molecule of claim 5, comprising SEQ ID NO:27 and SEQ ID NO:31.

51. (New) The binding molecule of claim 5, comprising SEQ ID NO:28 and SEQ ID NO:32.